DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of Public Health and Science and Food and Drug Administration

[Docket No. 2005N–0184]

Solicitation of Public Review and Comment on Research Protocol: Precursor Preference in Surfactant Synthesis of Newborns

AGENCY: ~~Office of Public Health and Science and~~ Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Office for Human Research Protections (OHRP), Office of Public Health and Science, Department of Health and Human Services (HHS), and the Food and Drug Administration (FDA), are soliciting public review and comment on a proposed research protocol entitled "Precursor Preference in Surfactant Synthesis of Newborns." The proposed research would be conducted at the St. Louis Children's Hospital and supported by the National Heart, Lung and Blood Institute. Public review and comment are solicited regarding the proposed research protocol under the requirements of HHS and FDA regulations.

DATES: To be considered, written or electronic comments on the proposed research must be received on or before 4:30 p.m. on June 17, 2005.

ADDRESSES: Electronic copies of the documents for public review can be viewed at the Pediatric Advisory Committee Docket Web site at *http://www.fda.gov/ohrms/dockets/ac/acmenu.htm.* (Click on the year 2005 and scroll down to Pediatric Ethics Subcommittee meetings.) Submit written comments to the Division of Dockets Management (HFA–305), Docket No.

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2005N–0184, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments.* All comments should be identified with the docket number found in brackets in the heading of this document. Received comments may be viewed on FDA's Web site at *http://www.fda.gov/ohrms/dockets/dockets/05n0184/05n0184.htm*, or may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Kevin Prohaska, Office for Human Research Protections, The Tower Building, 1101 Wootton Pkwy., suite 200, Rockville, MD 20852, 301–496–7005, FAX: 301- 402–2071, e-mail: *kprohask@osophs.dhhs.gov*; or Jan N. Johannessen, Office of the Commissioner (HF–33), Food and Drug Administration, 5600 Fishers Lane (for express delivery, rm. 14C–06), Rockville, MD 20857, 301–827–6687, or by e-mail: *jjohannessen@fda.gov.*

SUPPLEMENTARY INFORMATION: All studies conducted or supported by HHS that are not otherwise exempt and that propose to involve children as subjects require Institutional Review Board (IRB) review in accordance with the provisions of HHS regulations for the protection of human subjects in 45 CFR part 46, subpart D. Under FDA's interim final rule effective April 30, 2001, FDA adopted similar regulations in part 50, subpart D (21 CFR part 50, subpart D) to provide safeguards for children enrolled in clinical investigations of FDA-regulated products. Because the proposed research, "Precursor Preference in Surfactant Synthesis of Newborns," would be supported by NIH, a component of HHS, and would be regulated by FDA, both HHS and FDA regulations apply to this proposed research.

Under HHS regulations in 45 CFR 46.407, and FDA regulations in § 50.54, if an IRB reviewing a protocol to be conducted or supported by HHS for a clinical investigation regulated by FDA does not believe that the proposed research involving children as subjects meets the requirements of HHS regulations in 45 CFR 46.404, 46.405, or 46.406, and FDA regulations in §§ 50.51, 50.52, or 50.53, the research may proceed only if the following conditions are met: (1) IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and (2) the Secretary (HHS) and the Commissioner (FDA), after consultation with experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following opportunity for public review and comment, determine either: (a) That the research in fact satisfies the conditions of 45 CFR 46.404, 46.405, or 46.406 under HHS regulations, and §§ 50.51, 50.52, or 50.53 under FDA regulations, or (b) that the following conditions are met: (i) The research or clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; (ii) the research or clinical investigation will be conducted in accordance with sound ethical principles; and (iii) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 45 CFR 46.408 and 21 CFR 50.55.

HHS has received a request on behalf of the Washington University Medical Center IRB to review under 45 CFR 46.407 the protocol entitled "Precursor Preference in Surfactant Synthesis of Newborns." The principal investigator proposes to administer to preterm and full-term newborns simultaneous 24-hour infusions of palmitate and acetate labeled with the stable

(nonradioactive) isotope carbon-13, then measure the incorporation of each into surfactant, collected by tracheal aspiration. Subjects of the study would include approximately 10 full-term, intubated infants with normal lungs and 15 to 20 preterm (24 to 28 weeks gestational age), intubated infants with respiratory distress syndrome.

The overall goal of the proposed study is to better understand the potential differences in precursor preferences in surfactant synthesis between preterm infants with immature lungs (requiring mechanical ventilation) and full-term infants with normal lung function. The three specific aims of the study are to: (1) Determine the rate of surfactant synthesis using de novo synthesized fatty acids (acetate), (2) determine the rate of surfactant synthesis using preformed fatty acids (palmitate), and (3) compare the rates of incorporation in preterm infants versus full-term infants with normal lungs.

The Washington University Medical Center IRB determined that the protocol was not approvable under 45 CFR 46.404, 46.405, or 46.406 because the 24-hour isotope infusion and extra blood draws pose more than minimal risks to the subjects, there is no prospect of direct benefit to the individual subjects, the interventions or procedures do not present an experience to the control group that are reasonably commensurate with those inherent in their expected medical situation, and the control group does not have the condition or disorder under study. Accordingly, the Washington University Medical Center IRB forwarded the protocol to OHRP under 45 CFR 46.407 for consideration. Because this clinical investigation is regulated by FDA, FDA's regulations in part 50, subpart D, specifically § 50.54, apply as well.

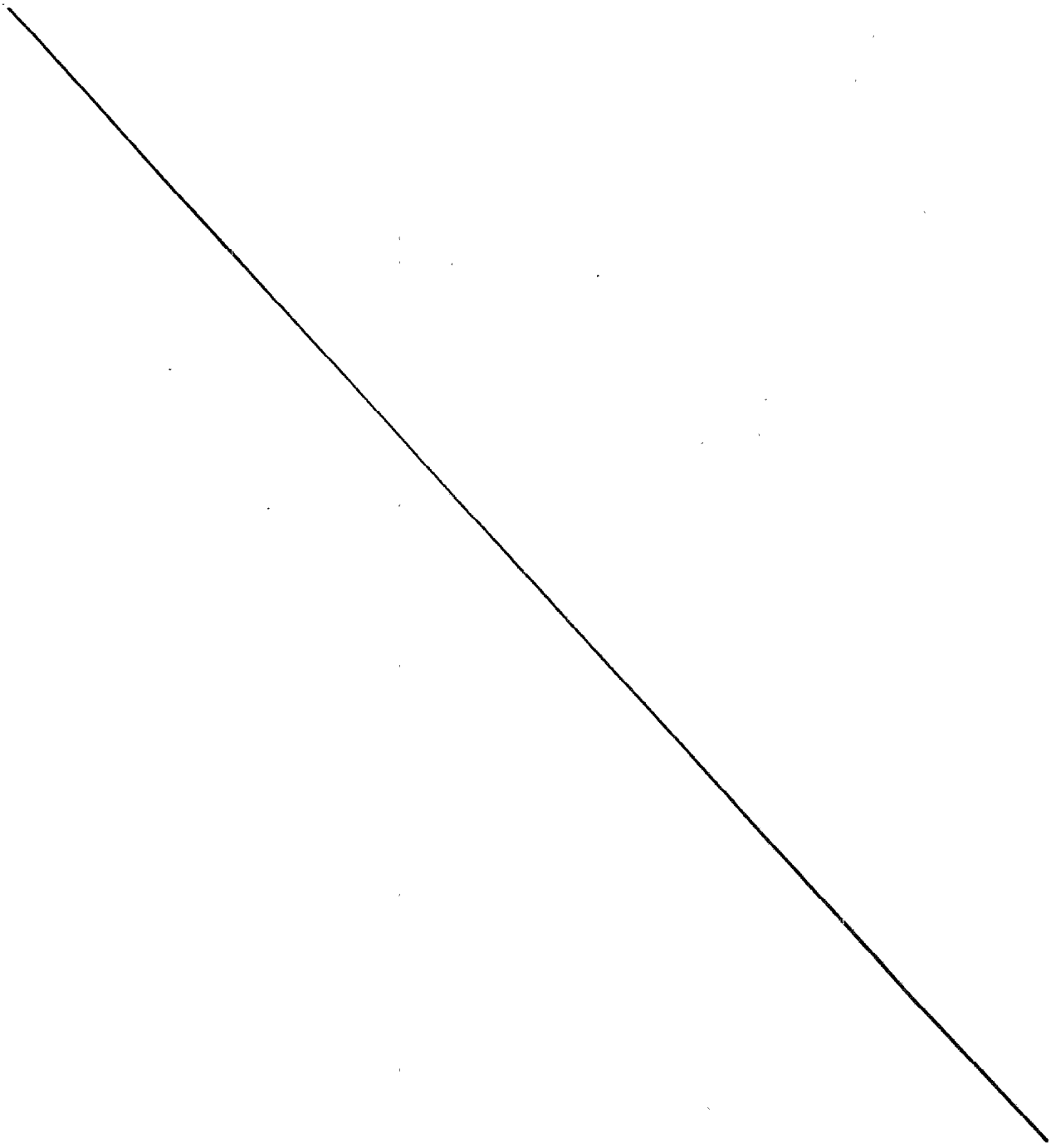
In accordance with 45 CFR 46.407(b) and 21 CFR 50.54(b), OHRP and FDA are soliciting public review and comment on this proposed clinical

investigation. In particular, comments are solicited on the following questions: (1) What are the potential benefits, if any, to the subjects and to children in general; (2) what are the types and degrees of risk that this research presents to the subjects; (3) are the risks to the subjects reasonable in relation to the anticipated benefits, and is the research likely to result in knowledge that can be generalized about the subjects' disorder or condition; and (4) does the research present a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

To facilitate the public review and comment process, FDA has established a public docket and placed in that docket information relating to the proposed clinical investigation, including the following: Correspondence from Washington University Medical Center referring the proposed research protocol to HHS for consideration under 45 CFR 46.407; correspondence from FDA and OHRP to Washington University Medical Center regarding the proposed protocol; the research protocol; NIH's grant funding the protocol; IRB's deliberations on the proposed research; the drug preparation protocol; certificate of analysis of the test compounds; the data safety monitoring plan; and the parental permission documents. Electronic copies of these documents can be viewed at the Pediatric Advisory Committee (PAC) Docket Web site at *http://www.fda.gov/ohrms/dockets/ac/acmenu.htm.* (Click on the year 2005 and scroll down to Pediatric Ethics Subcommittee meetings.) These materials are also available on OHRP's website at *http://www.hhs.gov/ohrp/children/.*

All written comments concerning this proposed research should be submitted to FDA's Division of Dockets Management under 21 CFR 10.20, no later than 4:30 p.m. on June 17, 2005. The background materials and received

comments may be viewed on FDA's Web site at *http://www.fda.gov/ohrms/dockets/dockets/05n0184/05n0184.htm* or may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday. The



background materials may also be viewed on OHRP's Web site at *http://www.hhs.gov/ohrp/children/.*

Dated: 5/19

May 19, 2005.

Sheila Dearybury Walcoff,
Associate Commissioner for External Relations.

[FR Doc. 05–????? Filed ??–??–05; 8:45 am]

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